A stimulating and informative course on the concepts and methods that are current in investigations concerning the chemistry of heredity was offered by the Third Annual Advanced Study Institute of Molecular Biology. The Institute was held on the island of Spetsai, Greece, July 4 through July 16, 1966. Dr. Marianne Grunberg-Manago (Paris) and Dr. A. Evangelopoulos (Athens) were responsible for arranging the Institute, which was sponsored by NATO with some financial assistance from the U. S. Office of Naval Research. The cooperation and generosity of the Greek government also contributed to the success of the Institute. The decision to hold this course in Greece stemmed from the growing interest and activity in molecular biology in that country, and a desire to stimulate that research by personal contact between Greek investigators and their foreign colleagues.

The five hours of lectures each day were held in the morning and evening. The facilities of a small college on Spetsai were used. Some 25 lecturers from Greece, Great Britain, France, Germany, Israel and the United States, each delivered between two and four one-hour lectures. These were followed by lively discussion periods, and the discussions continued through the afternoons and late evenings. Reading lists and brief abstracts for each lecture were distributed. The pleasant physical surroundings, the

absence of mechanized transportation, and the availability of dormitory and hotel space in close proximity fostered the maximum contact between students, and students and lecturers. The resulting atmosphere was similar to that found at a Gordon Conference. The 130 students (chosen from over 1000 applicants) represented 14 countries with the large majority from Western Europe, and Greece (twenty came from North America). They ranged from graduate students and recent graduates working in molecular biology, to established investigators working in related fields. The lectures assumed a basic knowledge of modern biochemistry and genetics and started with a general review of the experimental findings on which the latest concepts are based. Each speaker then presented the most recent findings from his own laboratory and since some of this work is among the most exciting and elegant being carried out in the field, a high level of scientific exuberance was maintained.

An initial talk by I. Photaki (Athens) on modern methods for the chemical synthesis of peptides was followed by a group of lectures on various aspects of the structure of nucleic acids. The electronic structure of mononucleotides and polynucleotides was discussed by B. Pullman (Paris). H. Boedtker (Harvard) and P. Doty (Harvard) spoke on the physical properties of RNA and DNA, respectively and gave particular emphasis to the problems inherent in the methods

that are available for studying these molecules in solution. Methods for obtaining and analyzing x-ray diffraction data for nucleic acids, thus yielding information on the overall three-dimensional configuration of these molecules, was discussed by R. Langridge (Cancer Research Foundation, Boston). A. M. Michelson (Paris) summarized the information on polynucleotide secondary structure that has been derived from studies with synthetic polymers. He stressed the fact that the physical properties characteristic of high molecular weight polynucleotides begin to develop even with dinucleotides. Michelson also concluded that the stacking of bases within the structure is, in large part, responsible for their stability and their optical properties, while hydrogen bonds control the specificity of base pairing. The specificity of the hydrogen bonding between purines and pyrimidines was further elucidated by A. Rich (M.I.T.) who described recent studies on crystalline complexes between derivatives of guanine and cytosine, and, similarly, adenine and uracil. M. Cohn (U. of Penn.) discussed the use of nuclear magnetic resonance in elucidating the nature of the interaction between an enzyme, divalent metal ion, and nucleotide.

J. Watson (Harvard) introduced the next group of lectures with a lucid description of current views on the mechanism of protein biosynthesis and in particular the variety of roles played by RNA in that process. He took special care to point out those areas

which are in need of concentrated work. Many of these areas were mentioned again in the talks that followed. Thus, R. Monier (Marseille) lectured on what is known and what is not known about the structure of the ribosome and its components, ribosomal RNA and protein. He also undertook the difficult job of summarizing and evaluating the literature relevant to the biosynthesis of ribosomes. Using his own recent work on the primary structure of two serine transfer RNAs from yeast as an example, H. Zachau (Köln) spoke on the primary and secondary structure of transfer RNA, emphasizing the relation of structure and function. Particularly useful for the students was his detailed description of the methodology used in work of this kind.

The biosynthesis of polyribonucleotides was the subject of several detailed lectures. J. Richardson (Paris) summarized the evidence that the DNA-dependent RNA polymerase is responsible for the synthesis of RNA within bacterial cells. Mentioning work from many laboratories, he described the details of the mechanism of this reaction which have been elucidated during the past year. M. Grunberg-Manago emphasized the consensus that polynucleotide phosphorylase is probably a degradative enzyme *in vivo*, and went on to describe recent studies with the highly purified enzyme from *E. coli*. U. Z. Littauer (Rehovoth) and A. Peterkofsky (N.I.H.) discussed enzymatically catalyzed structural modifications of polynucleotides. The former talked on the methylation of RNA and DNA while the latter

brought everyone up to date on the occurrence and synthesis of the thionucleotides in E. coli transfer RNA. Theories and experiments on the replication of viral RNA in vivo and in vitro, a subject which is under intensive study in several laboratories, was reviewd by H. Boedtker. The use of nucleases as analytical tools for the determination of the structure of naturally occurring and synthetic polynucleotides was covered in a lecture that I gave. I also discussed, in detail, the nucleases of E. coli and speculated on their respective physiological roles.

The next series of lectures concerned the mechanism of translation of messenger RNA. M. Grunberg-Manago gave a resume of work that led to the chemical description of the genetic code. The "wobble theory" of codon-anticodon recognition was presented by F.H.C. Crick (Cambridge, England) who also described experiments with so-called phase shift mutants of T_4 bacteriophage. These latter genetic experiments complement in vitro studies on the reading of the genetic code. Recent experiments on the initiation of polypeptide chain synthesis, which have led to the elucidation of specific initiator codons on messenger RNA and related transfer RNAs were described by B.F.C. Clark (Cambridge, England). This topic was discussed further by M. S. Bretscher (Cambridge, England), with particular reference to the binding of transfer RNA to ribosomes. Bretscher introduced the question of the mechanism of termination of

polypeptide chains, which was discussed in more detail by A. Garen (Yale). Garen's excellent lectures reviewed the genetic and biochemical data on bacterial suppression which have indicated a genetic control of the specificity of codon translation. Biochemical evidence that factors involved in this control are specific transfer RNAs, was presented by J. D. Watson in a talk which described *in vitro* protein synthesis in systems utilizing RNA from RNA-containing bacteriophage as messengers. A. Rich then reminded us that protein is made by organisms other than *E. coli* and its phage and presented a review of the role of polyribosomes in *in vitro* systems derived from reticulocytes as well as *E. coli*.

The regulation of protein biosynthesis was presented from several viewpoints. B. Ames (N.I.H.), using his own work on the histidine operon of *Salmonella* as an example, lectured on the general nature of the operon and theories of repression. E. Signer (M.I.T.) gave a review of the events that follow the infection of *E. coli* with virulent and temperate bacteriophage. A more general view of problems in the regulation of catabolic metabolism was given by I. C. Gunsalus (U. of Illinois) who also discussed the regulation of tryptophan biosynthesis in detail.

In recognition of the growing interest of many molecular biologists in the nervous system, E.S. Canellakis (Yale) concluded the Institute with a general review of the physiology and metabolism of the nerve cell.

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